

CLAIMS

We claim:

- 5           1. An immunoglobulin comprising a protection protein in association with an immunoglobulin derived heavy chain having at least a portion of an antigen binding domain.
- 10           2. The immunoglobulin of claim 1 further comprising an immunoglobulin derived light chain having at least a portion of an antigen binding domain associated with said immunoglobulin derived heavy chain.
- 15           3. The immunoglobulin of claim 1 or 2 further comprising a second immunoglobulin derived heavy chain having at least a portion of an antigen binding domain associated with said protection protein.
- 20           4. The immunoglobulin of claim 3 further comprising a second immunoglobulin derived light chain having at least a portion of an antigen binding domain bound to said second immunoglobulin derived heavy chain.
5. The immunoglobulin of claims 1-4 further comprising immunoglobulin J chain bound to at least one of said immunoglobulin derived heavy chains.
- 25           6. The immunoglobulin of claims 1-5 that is a therapeutic immunoglobulin.
7. The immunoglobulin of claim 6 wherein said therapeutic immunoglobulin binds to mucosal pathogen antigens.
- 30           8. The immunoglobulin of claim 7 that is capable of preventing dental caries.
9. The immunoglobulin of claims 1-8 wherein said antigen binding domain is capable of binding an antigen from S. mutans serotypes c, e and f or S.sobrinus serotypes d and g.
- 35           10. The immunoglobulin of claim 1 wherein said protection protein has an amino acid sequence which substantially corresponds to at least a portion of the

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amino acid residues 1 to 627 of the rabbit polyimmuno-  
globulin receptor and does not have an amino acid residue  
sequence corresponding to amino acid residues 628-755 of  
the rabbit polyimmunoglobulin receptor.

5 11. The immunoglobulin of claim 1 wherein said  
protection protein has an amino acid sequence which  
substantially corresponds to at least a portion of the  
amino acid residues 1 to 606 of the rabbit polyimmuno-  
globulin receptor and does not have an amino acid sequence  
10 corresponding to amino acid residues 628-755 of the rabbit  
polyimmunoglobulin receptor.

12. The immunoglobulin of claim 10 or 11 wherein  
said protection protein has an amino acid sequence which  
does not contain amino acid residues corresponding to  
15 amino acid residues 628 to 775 of the rabbit  
polyimmunoglobulin receptor and which does contain amino  
acid residues which correspond to one or more of the  
following amino acid segments:

- a) amino acids corresponding to amino acid resi-  
20 dues 21-43 of the rabbit polyimmunoglobulin receptor;
- b) amino acids corresponding to amino acid resi-  
dues 1 - 118 of the rabbit polyimmunoglobulin receptor;
- c) amino acids corresponding to amino acid resi-  
dues 119 - 223 of the rabbit polyimmunoglobulin receptor;
- 25 d) amino acids corresponding to amino acid resi-  
dues 224 - 332 of the rabbit polyimmunoglobulin receptor;
- e) amino acids corresponding to amino acid resi-  
dues 333 - 441 of the rabbit polyimmunoglobulin receptor;
- f) amino acids corresponding to amino acid resi-  
30 dues 442 - 552 of the rabbit polyimmunoglobulin receptor;
- g) amino acids corresponding to amino acid resi-  
dues 553 - 606 or 553 - 627 of the rabbit poly-  
immunoglobulin receptor.

13. The immunoglobulin of claim 1 wherein said  
35 protection protein has an amino acid sequence which does  
not contain amino acid residues of a polyimmunoglobulin  
receptor of a species which are analogous to amino acid

residues 628 to 755 of the rabbit polyimmunoglobulin receptor and which does contain amino acid residues from a polyimmunoglobulin receptor of a species which are analogous to one or more of the following amino acid segments:

- a) amino acids corresponding to amino acid residues 21 - 43 of the rabbit polyimmunoglobulin receptor;
- b) amino acids corresponding to amino acid residues 1 - 118 of the rabbit polyimmunoglobulin receptor;
- 10 c) amino acids corresponding to amino acid residues 119 - 223 of the rabbit polyimmunoglobulin receptor;
- d) amino acids corresponding to amino acid residues 224 - 332 of the rabbit polyimmunoglobulin receptor;
- e) amino acids corresponding to amino acid residues 333 - 441 of the rabbit polyimmunoglobulin receptor;
- 15 f) amino acids corresponding to amino acid residues 442 - 552 of the rabbit polyimmunoglobulin receptor;
- g) amino acids corresponding to amino acid residues 553 - 606 or 553 - 627 of the rabbit polyimmunoglobulin receptor.
- 20

14. The immunoglobulin of claim 13 wherein said species is human.

15. The immunoglobulin of claim 1 wherein said protection protein includes the amino acid sequence of at least one of the domains selected from the group consisting of the following portions of the rabbit polyimmunoglobulin receptor: domain I, domain II, domain III, domain IV, domain V, and amino acid residues 553 to 627 of domain VI; and does not have an amino acid sequence corresponding to amino acid residues 628-755 of the rabbit polyimmunoglobulin receptor.

16. The immunoglobulin of claim 1 wherein said protection protein does not have any amino acid sequence which corresponds to or is analogous to amino acid residues 628-755 of the rabbit polyimmunoglobulin receptor and which does include:

a) at least one domain which is from the polyimmunoglobulin receptor of a first animal and which is analogous to at least a portion of the following amino acid segments of the rabbit polyimmunoglobulin receptor: domain I,  
5 domain II, domain III, domain IV, domain V, and amino acid residues 553 to 627 of domain VI;

b) at least one domain which is from the polyimmunoglobulin receptor of a second animal and which corresponds to or is analogous to the following amino acid  
10 residue segments of the rabbit polyimmunoglobulin receptor: domain I, domain II, domain III, domain IV, domain V, and amino acid residues 553 to 627 of domain VI.

17. The immunoglobulin of claim 1 wherein said protection protein does not have any amino acid sequence  
15 which corresponds to or is analogous to amino acid residues 628-755 of the rabbit polyimmunoglobulin receptor and which does include:

a) at least one amino acid segment which is from the polyimmunoglobulin receptor of a first animal and which is  
20 analogous to at least a portion of the following amino acid residue segments of the rabbit polyimmunoglobulin receptor: domain I, domain II, domain III, domain IV, domain V, and amino acid residues 553 to 627 of domain VI;

b) at least one amino acid segment which is from  
25 the polyimmunoglobulin receptor of a second animal and which corresponds to or is analogous to the following amino acid residue segments of the rabbit polyimmunoglobulin receptor: domain I, domain II, domain III, domain IV, domain V, and amino acid residues 553 to 627 of domain VI.

30 18. The immunoglobulin of claim 16 wherein said first animal is a mammal and said second animal is a rabbit.

19. The immunoglobulin of claim 16 wherein said  
35 first animal is a human and said second animal is a rabbit.

20. The immunoglobulin of claim 1 wherein said immunoglobulin derived heavy chain contains at least a portion of an IgM or IgA heavy chain of any subtype.

21. The immunoglobulin of claim 1 wherein said immunoglobulin derived heavy chain is comprised of immunoglobulin domains from two different isotopes of immunoglobulin.

22. The immunoglobulin of claim 21 wherein said immunoglobulin domains are selected from the group consisting of:

a) the C<sub>H</sub>1 of a mouse IgG1 and the C<sub>H</sub>2 and C<sub>H</sub>3 of mouse IgA; and

b) the C<sub>H</sub>1 and C<sub>H</sub>2 of a mouse IgG1 and the C<sub>H</sub>2 and C<sub>H</sub>3 of mouse IgA;

23. The immunoglobulin of claim 1 wherein said antigen binding domain substantially corresponds to the Guy's 13 heavy chain variable region.

24. The immunoglobulin of claim 2 wherein said antigen binding domain substantially corresponds to the Guy's 13 light chain variable region.

25. The immunoglobulin of claim 1 wherein said protection protein has a first amino acid sequence which substantially corresponds to at least a portion of the amino acid residues 1 to 606 or 1 to 627 of the rabbit polyimmunoglobulin receptor and has a second amino acid residue sequence contiguous with said first amino acid sequence, wherein said second amino acid residue sequence does not have an amino acid residue sequence corresponding to the functional transmembrane segment of the rabbit polyimmunoglobulin receptor.

26. The immunoglobulin of claim 25 wherein said second amino acid residue sequence has an amino acid sequence which corresponds to amino acid residues 655 to 755 of a polyimmunoglobulin receptor.

27. The immunoglobulin of claim 25 wherein said second amino acid residue sequence is a portion of one or more of the following: an intracellular domain of a

polyimmunoglobulin molecule, a domain of a member of the immunoglobulin gene superfamily, an enzyme, a toxin, or a linker.

Sub 28. A eukaryotic cell containing an immunoglobulin  
5 of claims 1-24.

29. The eukaryotic cell of claim 28 wherein said eukaryotic cell is a plant cell.

30. The plant cell of claim 29 wherein said plant cell is part of a plant.

10 31. A eukaryotic cell containing a nucleotide  
Sub 2 sequence encoding a protection protein.

32. The eukaryotic cell of claim 31 which also contains a second nucleotide sequence encoding at least one of the molecules selected from the group consisting of: an immunoglobulin derived heavy chain having at least a portion of an antigen binding domain, an immunoglobulin derived light chain having at least a portion of an antigen binding domain, or an immunoglobulin J chain.

33. The eukaryotic cell of claim 32 wherein said  
20 second nucleotide sequence encodes an immunoglobulin derived heavy chain having at least a portion of an antigen binding domain; and which also contains a third nucleotide sequence encoding an immunoglobulin derived light chain having at least a portion of an antigen  
25 binding domain.

34. The eukaryotic cell of claim 33 which also contains a fourth nucleotide sequence encoding an immunoglobulin J chain.

35. The eukaryotic cell of claims 31-34 wherein  
30 said eukaryotic cell is a plant cell.

Sub 3 36. A plant cell containing a nucleotide sequence encoding a protection protein and a nucleotide sequence encoding an immunoglobulin derived heavy chain having at least a portion of an antigen binding domain.

37. A eukaryotic cell containing a protection protein.

38. The eukaryotic cell of claim 37 which also contains at least one additional molecule selected from the group consisting of: an immunoglobulin derived heavy chain having at least a portion of an antigen binding domain, an immunoglobulin derived light chain having at least a portion of an antigen binding domain, or an immunoglobulin J chain.

39. The eukaryotic cell of claim 38 wherein said additional molecule is an immunoglobulin derived heavy chain having at least a portion of an antigen binding domain; and which also contains an immunoglobulin derived light chain having at least a portion of an antigen binding domain.

40. The eukaryotic cell of claim 37 which also contains an immunoglobulin J chain.

41. The eukaryotic cell of claims 37-40 wherein said eukaryotic cell is a plant cell.

42. The plant cell of claims 29, 35, 36 and 41 wherein said plant cell is derived from a dicotyledonous or monocotyledonous plant.

43. The plant cell of claims 29, 35, 36 and 41 wherein said plant cell is derived from a solanaceous plant.

44. The plant cell of claims 29, 35, 36 and 41 wherein said plant cell is alfalfa cell.

45. The plant cell of claims 29, 35, 36 and 41 wherein said plant cell is derived from a tobacco plant.

46. The plant cell of claims 29, 35, 36 and 41 wherein said plant cell is part of a plant.

47. A composition comprising an immunoglobulin of claims 1-24 and plant macromolecules.

48. The composition of claim 47 wherein the plant molecules are derived from a dicotyledonous, monocotyledonous, solanaceous, alfalfa or tobacco plant.

49. The composition of claim 47 wherein said plant molecules are ribulose biphosphate carboxylase, light

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50. The composition of claim 47 wherein said immunoglobulin is present in a concentration of between 0.001% and 99% mass excluding water.

52. A method of producing an immunoglobulin of  
10 claims 1-24 comprising the steps of:

15 (b) introducing into said plant cell an expression vector containing a nucleotide sequence encoding an immunoglobulin derived heavy chain having at least a portion of an antigen binding domain operably linked to a transcriptional promoter.

(c) introducing into said plant cell an expression vector containing a nucleotide sequence encoding an immunoglobulin derived light chain having at least a portion of an antigen binding domain operably linked to a transcriptional promoter.

55. The method of claims 52-54 wherein said immunoglobulin derived heavy chain is immunoglobulin alpha chain and said immunoglobulin derived light chain is an immunoglobulin kappa or lambda chain.



a) introducing into a eukaryotic cell nucleotide sequences operably linked for expression encoding:

- 5
- i) an immunoglobulin derived heavy chain having at least a portion of an antigen binding domain,
  - ii) an immunoglobulin derived light chain having at least a portion of an antigen binding domain,
  - iii) an immunoglobulin J chain, and
  - iv) a protection protein; and
- b) maintaining said cell under conditions allowing
- 10 production and assembly of said immunoglobulin derived heavy and light chains, said immunoglobulin J chain and said protection protein into an immunoglobulin molecule.

67. A method for producing an assembled immunoglobulin molecule having heavy, light and J chains and a

15 protection protein by maintaining under conditions allowing protein production and immunoglobulin assembly, a eukaryotic cell containing nucleotide sequences operably linked for expression encoding:

- 20
- i) an immunoglobulin derived heavy chain having at least a portion of an antigen binding domain,
  - ii) an immunoglobulin derived light chain having at least a portion of an antigen binding domain,
  - 25 iii) an immunoglobulin J chain, and
  - iv) a protection protein.

68. The method of claims 66-67 wherein said eukaryotic cell is a plant cell.

69. A method of making an immunoglobulin resistant

30 to environmental conditions comprising the steps of :

- a) operably linking a nucleotide sequence encoding at least a portion of the antigen binding domain derived from an immunoglobulin heavy chain to a nucleotide sequence encoding at least one domain derived from an immunoglobulin
- 35 alpha heavy chain to form a nucleotide sequence encoding a chimeric immunoglobulin heavy chain;

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30           b)    at least one other molecule selected from the  
                  group consisting of: a protection protein, an  
                  immunoglobulin derived light chain having at  
                  least a portion of an antigen binding domain  
                  and an immunoglobulin J chain;  
35   thereby allowing the chimeric immunoglobulin heavy chain  
     to assemble with said at least one other molecule to form

5 73. A tetratransgenic organism comprised of cells

10 74 The transgenic organism of claim 72 wherein at

75 The transgenic organism of claim 73 wherein at

76 The transgenic organism of claim 73 wherein at

77 The transgenic organism of claim 73 wherein at

79 The transgenic organism of claim 73 wherein at

70 The transgenic organism of claim 73 wherein

80 The transgenic organism of claim 73 wherein

21 The immunoglobulin of claim 1 wherein said

82 The immunoglobulin of claim 81 wherein said

83. The immunoglobulin of claim 81 wherein said protection protein-binding domain is from the IgA of a human, rodent, rabbit, bovine, ovine, canine, feline or primate.

85. The immunoglobulin of claim 81 wherein said chimeric immunoglobulin heavy chain is comprised of immunoglobulin domains of a human IgG, IgM, IgD or IgE and said protection protein-binding domain is from a human IgA or IgM.

15 or ~~IgM.~~

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